

3. (Amended) A [Method] method of screening according to Claim 1 [or Claim 2], characterized in that in step a) the said NCTA is administered by the intraperitoneal route, at a dose corresponding to an inoculum of NCTA, between 0.001% and 10% (weight/volume) ( $LD_{50}$  between  $10^3$  and  $10^7$ ).

4. (Amended) A [Method] method of screening according to [any one of Claims 1 to 3,] Claim 1, characterized in that in step d) the said method of isolation is selected such that the ratio: maximum level detectable in the spleen/cut off is greater than 2 or such that a  $\frac{1}{2}$  dilution of the final sample obtained still provides a detection signal.

5. (Amended) A [Method] method of screening according to [any one of Claims 1 to 4,] Claim 1, characterized in that in step d) the said method of isolation of PrPres comprises a separation in a single step.

6. (Amended) A [Method] method of screening according to [any one of Claims 1 to 4,] Claim 1, characterized in that in step e) the PrPres is detected by immunoassay.

7. (Amended) A [Method] method of isolating PrPres, from an organ or a tissue, in particular the spleen or the brain, which is capable of being used in a method according to [any one of Claims 1 to 6,] Claim 1, characterized in that it comprises essentially the following steps:

(i) homogenization of organ or tissue, collected after sacrificing the animal, by mechanical grinding in a homogenization buffer, followed by calibration of the homogenate, for the production of a homogenate comprising, in weight/volume, from 5 to 50% of the said organ or tissue;

(ii) specific extraction of PrPres comprising a single separation step, by treating the homogenate obtained in step (i) by incubating the suspension obtained with a protease and an anionic detergent capable of promoting the aggregation of the PrPres in a suitable buffer and separation of the PrPres, by a single ultracentrifugation at 480,000-1,200,000 g.h, preferably for 2-4 hours, for example at 240,000- 300,000g for 2 to 4h, preferably at 20-22°C, of the said suspension, deposited on a buffer cushion having a density of between 1.02 and 1.08, at 20°C and recovering the centrifugation pellet comprising the said PrPres; and, if necessary,

(iii) purification of the PrPres by suspending the centrifugation pellet obtained in (ii) in a Laemmli buffer comprising 1-5% SDS, incubating in this buffer at 100°C for 2-10 minutes and centrifuging at 12,000-15,000 g for 10-15 minutes at 16-22°C.

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8. (Amended) A [Method] method of isolating PrPres, from an organ or a tissue, in particular the spleen or the brain, which is capable of being used in a method according to [any one of Claims 1 to 6,] Claim 1, characterized in that it comprises essentially the following steps:

(i) homogenization of organ or tissue, collected after sacrificing the animal, by mechanical grinding in a homogenization buffer, followed by the addition, to the homogenate obtained, of a salt having a high ionic strength and capable of promoting the aggregation of the PrPres in a 1:1 (v/v) ratio, followed by calibration of the homogenate, for the production of a homogenate comprising, in weight/volume, from 5 to 50% of the said organ or tissue;

(ii) specific extraction of PrPres by treating the homogenate obtained in step (i) by incubating the suspension obtained with solution comprising a protease and an anionic detergent capable of promoting the aggregation of the PrPres, and a single separation of the PrPres, by centrifugation at 25,000-60,000 g.h, for example at 25,000-30,000 g for 1 to 2 h, preferably at 16-22°C, of the suspension obtained, deposited on a buffer cushion having a density of between 1.02 and 1.08, at 20°C, and recovering the centrifugation pellet comprising the said PrPres; and, if necessary,

(iii) purification of the PrPres by suspending the centrifugation pellet obtained in (ii) in a Laemmli buffer comprising 1-5% SDS, incubating in this buffer at 100°C for 2-10 minutes and centrifuging at 12,000-15,000 g for 10-15 minutes at 16-22°C.

9. (Amended) A [Method] method according to Claim 7 [or 8], characterized in that the homogenization buffer in step (i) is in particular a neutral buffer such as water or an isotonic buffer such as 5% glucose.

10. (Amended) A [Method] method according to Claim 7 [or Claim 8], characterized in that in step (ii), prior to the centrifugation, at least one protease inhibitor is added.

11. (Amended) A [Method] method according to Claim 7 [or Claim 8], characterized in that in step (ii) the centrifugation is preferably carried out after depositing the suspension containing the PrPres on a 6-20% sucrose cushion.

12. (Amended) A [Method] method according to Claim 8, characterized in that during the extraction step (ii) the solution used for the extraction comprises an anionic detergent capable of promoting the aggregation of the PrPres and a zwitterionic detergent, such as a sulphobetaine, preferably the sulphobetaine SB 3-14 at 1-2%, in a 1:1 (v/v) ratio.

13. (Amended) A [Method] method according to Claim 8, characterized in that in the extraction step (ii) the centrifugation is preferably carried out after depositing the suspension containing the PrPres on a cushion comprising, in a mixture, 6-20% sucrose and a sulphobetaine.